Our patient was then compared with those of subjects with normal renal function [1]. Influence of haemodialysis was also studied with calculation of the extraction ratio E and the haemodialysis clearance CL_{HD}. Moreover, we determined the significance of haemodialysis clearance as compared with total body clearance: F_{HD} [CL_{HD} / (CL_{HD} + CL_{ER})] where CL_{ER} is ‘extra-renal’ clearance [7].

Neither clinical (nausea, rash, diarrhoea, abdominal pain or vomiting) nor biological [hyperlipidaemia, elevation of serum transaminases (ASAT: 30 and 32 IU/l; ALAT: 25 and 21 IU/l, respectively) and unconjugated hyperbilirubinaemia] side effects were observed.

Our pharmacokinetic parameters are summarized in Table 1.

| Dose (mg) | 400 | 400 |
| Dosing interval (h) | 24 | 24 |
| Pharmacokinetics | | |
| C_{max} (ng/ml) | 4855 | 2918–5867 |
| T_{max} (h) | 4 | 2–4 |
| C_{min} (ng/ml) | 375 | 149–219 |
| AUC (ng - h/l) | 49 800 | 18 590–33 500 |
| T_{1/2} (h) | 7.19 | 5.28 |
| CL_{F} (ml/min) | 134 | 420 |
| V_{d/F} (l) | 83.4 | 109–187 |
| Haemodialysis | | |
| E (%) | 14 | |
| CL_{HD} (ml/min) | 40 | |
| F_{HD} (%) | 23 | |

Table 1. Pharmacokinetic parameters of atazanavir in a haemodialysed HIV-1-infected patient

Additional analysis of atazanavir pharmacokinetics was performed on the haemodialysed patient (off-dialysis day) and during the two haemodialysis sessions. Atazanavir concentrations were 2198 and 1807 ng/ml before and after haemodialysis, respectively. Two hours after the start of haemodialysis, arterial and venous concentrations were 2183 and 1881 ng/ml, respectively. Values of E and CL_{HD} of atazanavir were 14% and 40 ml/min, respectively. F_{HD} was 23%, i.e. below the 25% limit value above which haemodialysis clearance should be considered clinically significant.

Our results showed that atazanavir pharmacokinetics differed in our haemodialysis patient as compared with reference values in patients with normal renal function. However, in this case, atazanavir was associated with both efavirenz and ritonavir. Such an association has been reported to induce a 40% increase in atazanavir AUC in patients with normal renal function [1]. Indeed, the AUC increase observed in our patient was most likely due to the coadministration of efavirenz and ritonavir rather than secondary to renal failure-induced pharmacokinetic alterations.

This increased AUC, thus, resulted in a decreased CL/F and an increased T_{1/2}.

From these data, we suggest that atazanavir should be administered at its normal dosage in patients with renal insufficiency undergoing haemodialysis. Furthermore, atazanavir seems not to be significantly dialysable and administration may, thus, be performed anytime before or after the session on haemodialysis days. However, further studies would be needed to confirm these preliminary results.

Conflict of interest statement. None declared.

1Department of Nephrology
2Department of Pharmacology
3Department of Infectious Diseases

Gemella morbillorum peritonitis in a patient being treated with continuous ambulatory peritoneal dialysis

Sir,

Peritonitis is a serious problem for peritoneal dialysis (PD) patients, and is a major cause of hospitalization, catheter loss and transfer to haemodialysis [1]. We present a peritonitis episode caused by an unusual pathogen, Gemella morbillorum. A 55-year-old man was admitted to hospital after noticing his dialysis effluent was slightly cloudy. He received three exchanges of 1.36% and one exchange of 2.27% 2000 ml of

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PD solution (Baxter-Dianeal 137, Deerfield, IL) in a day. He had no prior history of peritonitis. The clinical picture was dominated by mild diffuse abdominal pain and tenderness. Analysis of the peritoneal effluent demonstrated a white blood cell (WBC) count of 480/μl with 90% neutrophils. Gram stain of the effluent revealed no bacteria. Culture of the specimen grew slow-growing, Gram-positive, pleomorphic, catalase-negative bacteria that were identified as Gemella morbillorum. The minimal inhibitory concentrations determined by E Test® for penicillin and vancomycin were 0.006 and 1 mg/l, respectively, which were interpreted as susceptible. Prior to identification of the bacteria, ampicillin–sulbactam (1.5 g bid) and ciprofloxacin (200 mg bid) were started intravenously as the regular therapy for CAPD peritonitis in our institution, and the same combination continued for 14 days. The WBC of the peritoneal effluent dropped to zero at the end of the first week of therapy. The patient was well when he was seen 1 month after his discharge.

Gemella morbillorum and Gemella hemolysans are Gram-positive coccal commensal organisms of the mucous membranes of humans. Only a few cases of Gemella infection have been reported to date, and have been predominantly endovascular infections [2]. The first episode of peritonitis caused by G. morbillorum was successfully treated with cefazolin [3].

Gemella may be more involved in clinical disease than is presently recognized. They can be incorrectly identified as viridans streptococci, identified as Neisseria spp. because they are easily decolorized during Gram staining or left unidentified [2]. Our patient had no other underlying disease besides end-stage renal failure and no other infectious focus prior to this peritonitis episode. Translocation from the gastrointestinal tract may be responsible for this episode. We did not culture the stool of the patient before antimicrobial therapy to demonstrate Gemella. It is difficult to estimate how this microorganism caused this episode.

Gemella infections are seldom seen, and the identification in the laboratory has some limitations because of the characteristics of this bacteria. Therefore, the microbiological samples should be interpreted carefully and Gemella should be taken into consideration when slow-growing, catalase-negative, Gram-positive cocci are seen in samples. There are fatal Gemella infection reports in the literature [4,5]. Our case improved well with a β-lactum antibiotic as in the other patient mentioned above [3]. The response of two patients to therapy is not enough to reach a general conclusion about the prognosis, but the in vitro susceptibility results may be a useful guide in the management of these patients.

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Baskent University
Faculty of Medicine
Infectious Disease and Clinical Microbiology
Ankara
Turkey
Email: okurtazap@baskent-ank.edu.tr


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Measurement of cyclosporin exposure in renal transplant recipients during the early post-operative period: is C2 alone sufficient?

We note the association between achievement of target C2 [the 2 h post-dose blood cyclosporin (CsA) concentration] values and a lower incidence of acute renal transplant rejection reported by di Paolo et al. [1]. This is supported by other studies [2,3]. The authors also state that target C2 was not achieved during the early post-operative period in a significant proportion of patients, despite using high doses of Neoral®. The experience with C2 monitoring in our unit has been very similar, but our data also suggest that C2 is not a reliable measure of CsA exposure in the first week post-transplantation.

Having demonstrated an association between C2 and acute rejection (AR) in a retrospective study of patients in whom CsA dose adjustment was based solely on trough blood CsA levels (C0) [4], we introduced a target-driven protocol for CsA dose adjustment that was based primarily on C2 but also C0 and various clinical factors (see below). The protocol was applied to 60 consecutive renal transplant recipients (36 male, 55 Caucasian, age 45.9 ± 13.6 years, four with diabetes mellitus, time on renal replacement therapy 59.3 ± 49.4 months, 51 first grafts). The donor profile was as follows: 28 male, age 47.7 ± 16 years, 10 living/ 50 cadaveric. The mean number of human leukocyte antigen mismatches was A 0.79 ± 0.53, B 0.89 ± 0.54 and DR 0.19 ± 0.44. The standard immunosuppressive regimen comprised Neoral®, prednisolone and azathioprine (AZA), but 10 patients at high immunological risk received mycophenolate mofetil in place of AZA. Neoral® was commenced at 10 mg/kg/day in divided doses and then adjusted according to C2 values (for doses 4/5 and then every fourth dose until hospital discharge, target range 1350–1650 ng/ml). Neoral® dose increases for patients with suboptimal C2 values were waived if paired C0 values exceeded 500 ng/ml or there was delayed graft function and/or clinical evidence of CsA nephrotoxicity.

The incidence of acute allograft rejection (biopsy-proven or suspected on clinical grounds with a good response to increased immunosuppression) within the first 20 days post-transplant was 10%. Delayed graft function occurred in 33.3% of cases. The incidence of adverse events was as follows: hepatitis [alanine aminotransferase >50 IU/l] 27%, hyperbilirubinemia (serum bilirubin >30 μmol/l) 27%, haemolytic uraemic syndrome 3.3%, CsA nephrotoxicity (with improvement in serum creatinine following CsA dose reduction) 8.3%. Target range C2 values were achieved in 42, 67 and 67% of patients by days 3, 5 and 7, respectively. There was a non-significant trend towards a lower incidence...